## REMARKS

Applicants respectfully request reconsideration and withdrawal of the rejections set forth in the Office Action. As requested by the examiner, paragraphs 0017, 0019, 0020, 0024, 0067, 0078, 0098, and 0103 of the specification were amended to reference the correct figures and to place the paragraphs in proper form.

Claims 1- 8 were pending in the above reference application. Claim 1 has been amended. Claims 6-8 were withdrawn from consideration. Additionally, Applicants have added new claims 9-11. Exemplary support for these new claims exist in the specification at page 5, paragraphs 11-12; page 6, paragraph 14; and page 20, paragraph 69.

Because the foregoing amendments and new claims do not introduce new matter, entry of them by the Examiner is respectfully requested. Upon entry of this changes, claims 1-5, and 9-11 will be pending in the application.

**Rejection of Claims under 35 USC §112**

Claims 1-5 are rejected under 35 USC §112, first paragraph for lack of enablement and 35 USC §112, second paragraph for indefiniteness. Amended claims 1-5 recite specific sequences, which should address the Examiner's stated concerns regarding the prior art and §112 rejections, respectively.

The amended claims recite the phrase "mammalian homolog," which is amply supported in the specification. For example, the specification discloses the similarity of mouse, human and rat promoter regions for GLP-2R. See specification at Figure 7b described on page 7 paragraph 24, and specification at page 11 paragraph 45 and 46. In both the human genome and the rat genome, the promoter region comprises at least 1.5 kb upstream from the start codon in the genomic DNA representing the GLP-2R gene. This similarity displays the evolutionary homology of the GLP-2R promoter region between these species. Further, because transcription regulation is limited to a few sequences within the regulatory region, base changes in non-critical sequences produce minimal changes in gene expression. Therefore, the slight base changes between the mammalian homologs in the promoter region will not alter the gene expression or disrupt the gene's regulatory function, as stated in the specification on page 11 paragraph 46.

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner also is invited to contact the undersigned, should any issue require further consideration.

Respectfully submitted,

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Date

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**Versions with Markings to Show Changes Made**

**IN THE SPECIFICATION**

Please amend the Specification as follows:

Please replace paragraphs 0017, 0024, 0067, 0098 and 0103 with the following rewritten paragraphs, respectively:

[0017] **Figures 1a-1c provide** ~~**[Figure 1 provides]**~~ the nucleotide sequence of a 5'-flanking and 5'-untranslated region (UTR) of a GLP-2 receptor gene.

[0019] ~~**[Figure 3 illustrates]**~~ **Figures 2, 7a, and 7b illustrate** the strategy employed to amplify the 5'UTR of rat GLP-2 cDNA and identify a counterpart murine UTR.

[0024] Figure 7b shows the organization of a 5'-flanking and exon-1 sequences in the mouse GLP-2R gene (SEQ ID NO: 6 and 9) compared to rat exon-1 (**SEQ ID NO: 6** ~~**[SEQ ID NO: 7]**~~) and human GLP-2R (**SEQ ID NO: 7** ~~**[SEQ ID NO: 8]**~~) 5'-flanking and 5'-untranslated sequences.

[0067] The candidate modulating agents can be identified within vast chemical libraries, using a random screening approach. Particularly suitable agents for screening are those agents known to have an effect on the binding, to the GLP-2R promoter, of transcriptional factors that influence the function of that promoter. The identification of these transcription factors, and the sequence motif within the promoter region to which they bind, can be accomplished using established algorithms. One such program useful to identify these motifs and corresponding transcription factors is known as TFSEARCH~~**[, and is available on line at http://pdap1.trc.rwap.or.jp/h1bin/nph-tfsearch]**~~. The application of this algorithm to the sequence illustrated in Figure 1 has revealed numerous motifs and their corresponding transcription factors. Accordingly, and in a more directed approach to the identification of GLP-2R promoter modulators, these binding interfaces can be targeted for either augmentation or interference. Compounds already known to modulate these specific interactions qualify as GLP-2R promoter modulators.

- - [0078] The relative positions of the oligonucleotide primers designed for the primer extension and 5'-RACE reaction ~~**[are indicated in the shaded boxes of Figure 2]**~~ **were identified**. The results of the primer extension reaction and position of the oligonucleotide primer used for the nested 5'-RACE reaction predicted a 500-basepair (bp) product. A 500-bp product was cloned and sequenced using 5'-RACE reactions. The 5' end of the cDNA encoding the rat GLP-2R contains two putative translation

initiation ATG codons, 126-bp apart. The putative tss (transcriptional start site) maps to approximately –230 bp upstream of the second ATG codon in both rat and mouse transcripts encoding the GLP-2R.

[0098] Figure 7c shows construction of the transgene achieved by inserting a 1.5-kb Sma l-Pst l fragment of the murine GLP-2R gene upstream of an nlsLacZ cDNA. The **shaded** ~~**[solid black]**~~ box denotes the presence of GLP-2R 5'-untranslated sequences (5'-UTR) 5'-to the PST l site shown in Figure 7b.

[0103] As the glucagon, GLP-1, and GLP-2 receptors are related members of a G protein coupled receptor superfamily (Sherwood et al.,(2000) *Endocr Rev* **21**(6), 619-70), the sequences of the 5'-untranslated and 5'-flanking regions of these 3 receptors were compared. Significant similarity was not found using base-pair matching over 5'-untranslated or putative promoter regions. No putative TATA or CAAT box sequences were identified in the mouse GLP-2R genomic sequences immediately 5'- to the end of the putative 5'-untranslated region. Computer analyses identified several potential transcription factor recognition sites (TFSEARCH ver.1.3~~[; http://pdap1.trc.rwcp.or.jp/research/db/TFSEARCH.html]~~) for CdxA, GATA-1, NF-Kappa B, and Sp1, as indicated in Figure 7b.

**Versions with Markings to Show Changes Made**

**IN THE CLAIMS**

1. (Amended) A recombinant DNA construct, comprising a promoter region of a GLP-2 receptor gene and, linked for expression therewith, a heterologous gene of interest, **wherein the promoter region comprises at least the last 1,000 nucleotides of (A) the murine nucleotide sequence of SEQ ID NO. 1 or (B) a mammalian homolog of said murine nucleotide sequence**.